

FIG. 2.0

b. a. \ominus



\oplus

FIG 21

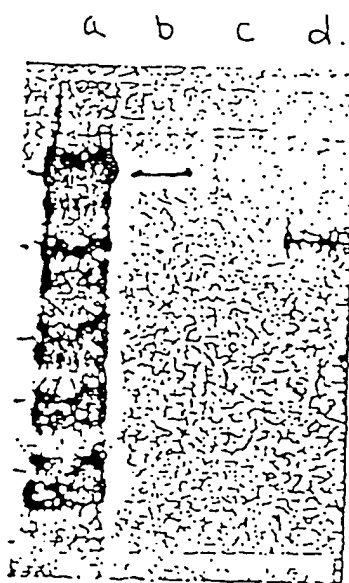


FIG. 22

a b c d.

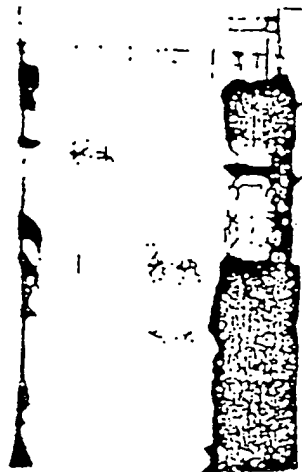


FIG 23

a. b.

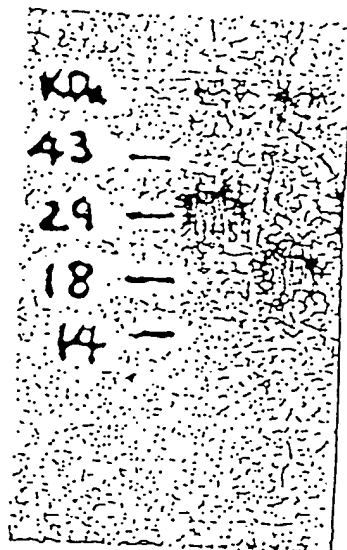
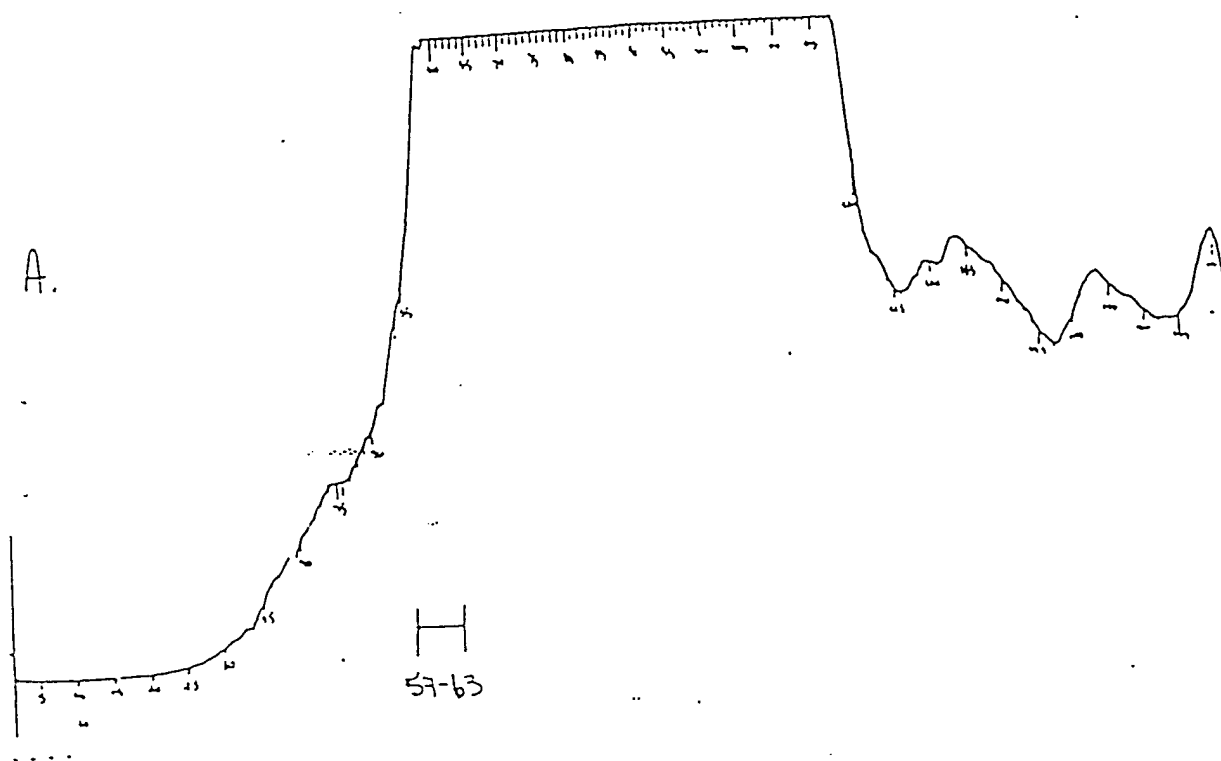


FIG. 24

Figure 6



B.

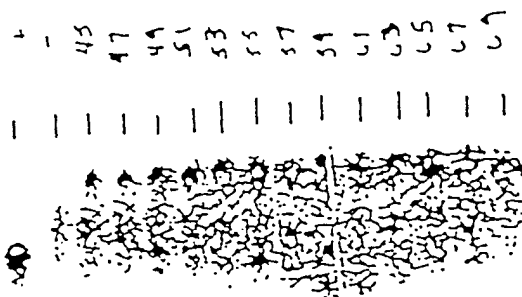
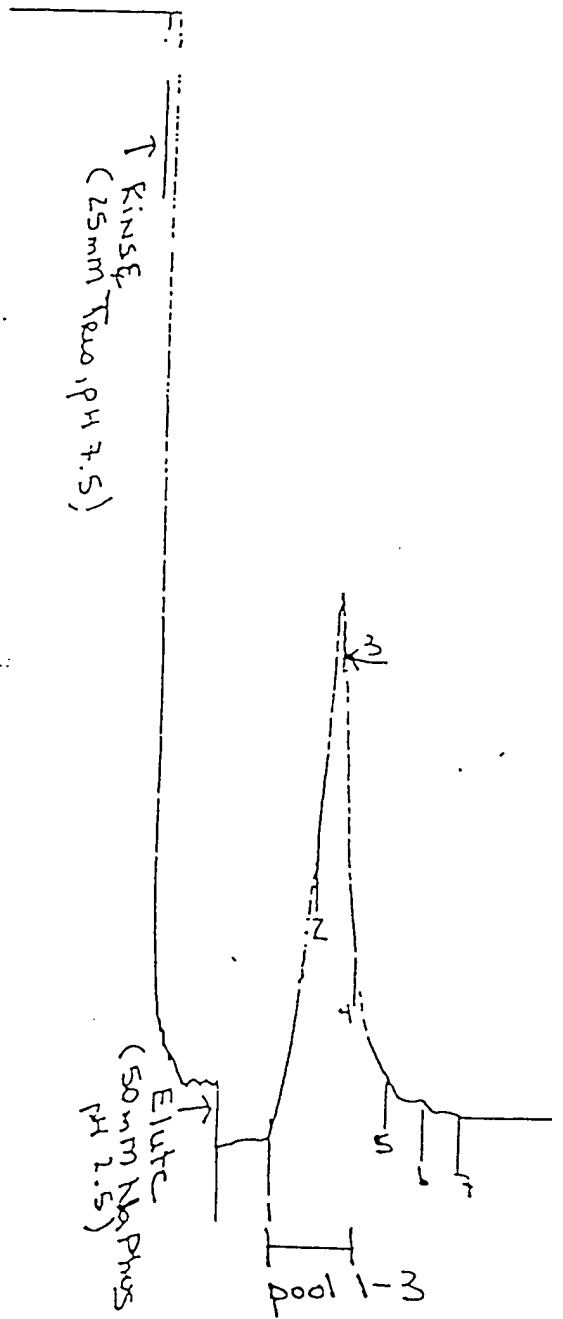


Figure 26



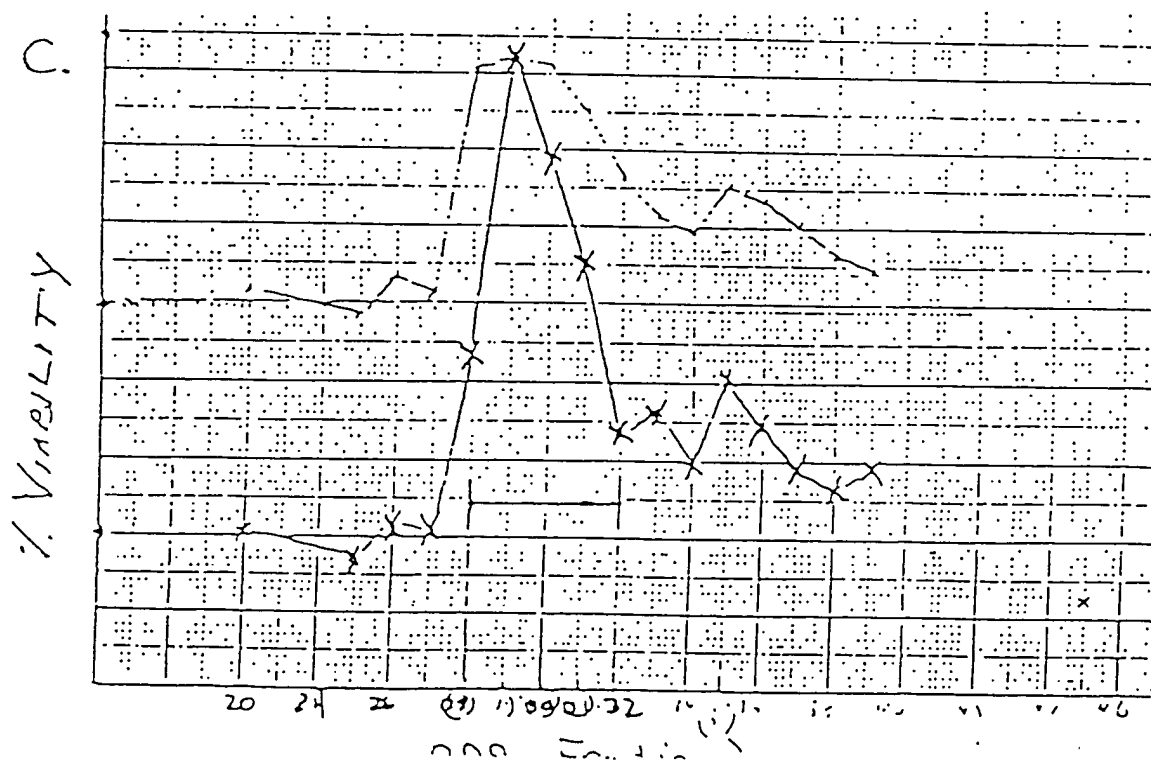
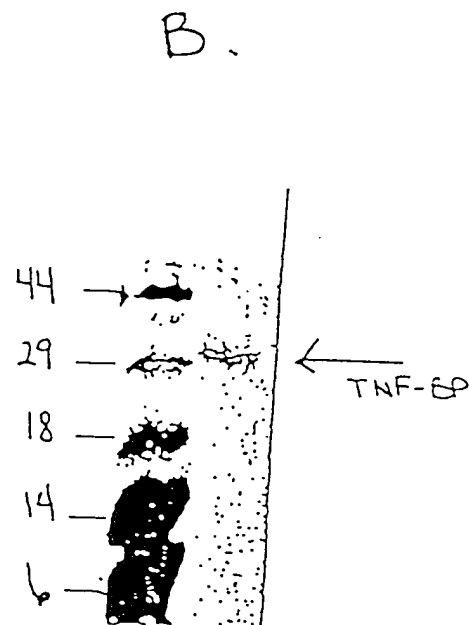
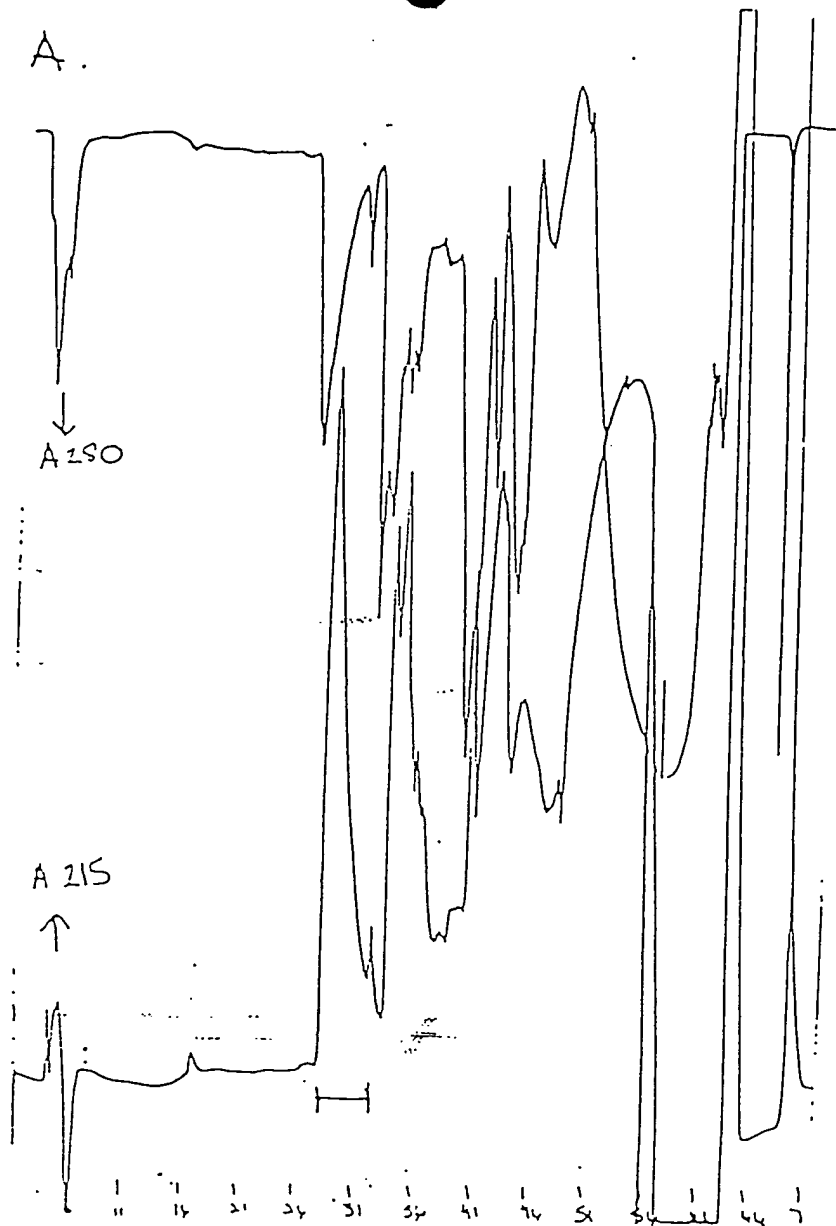


FIG. 28A

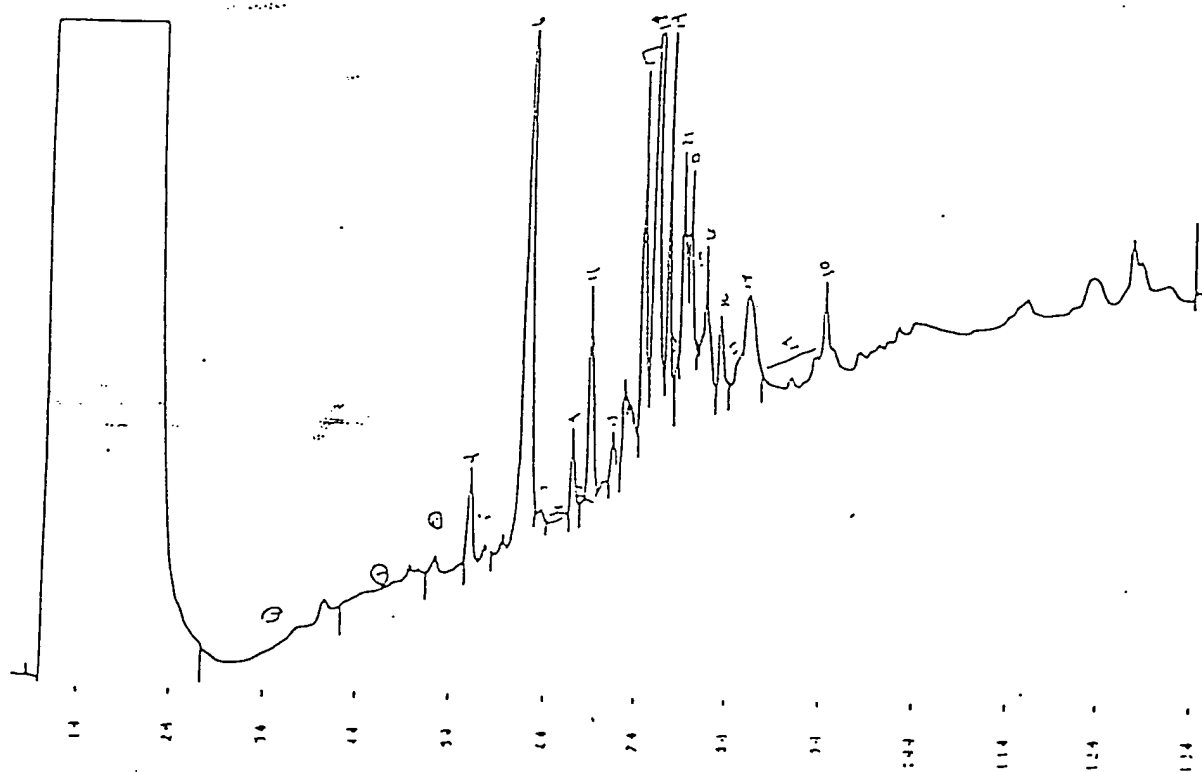
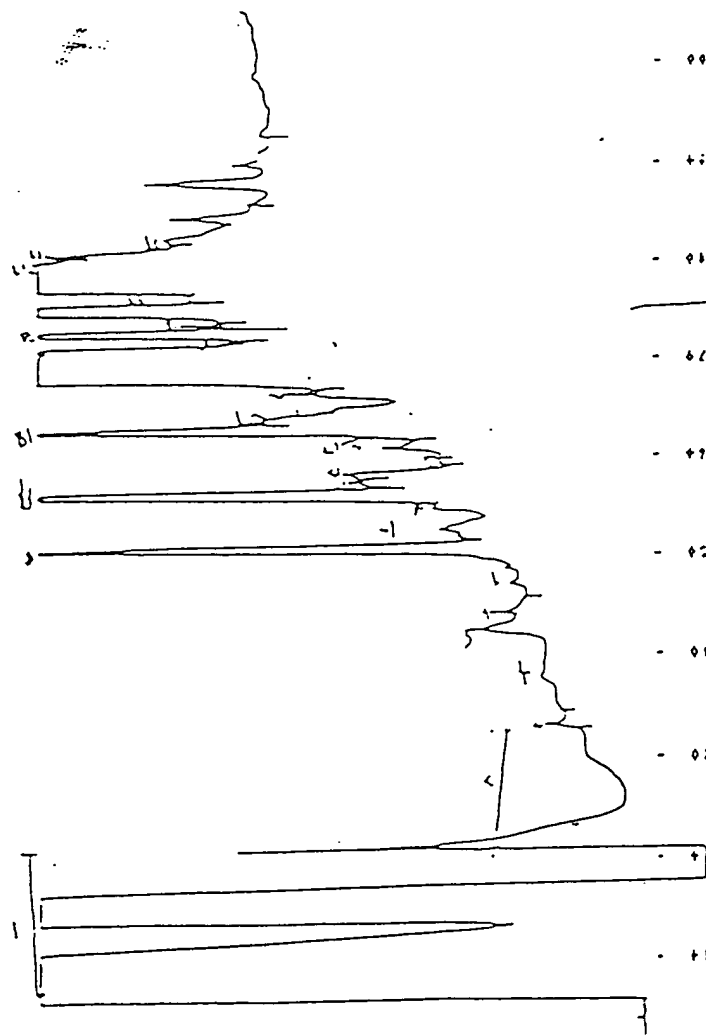
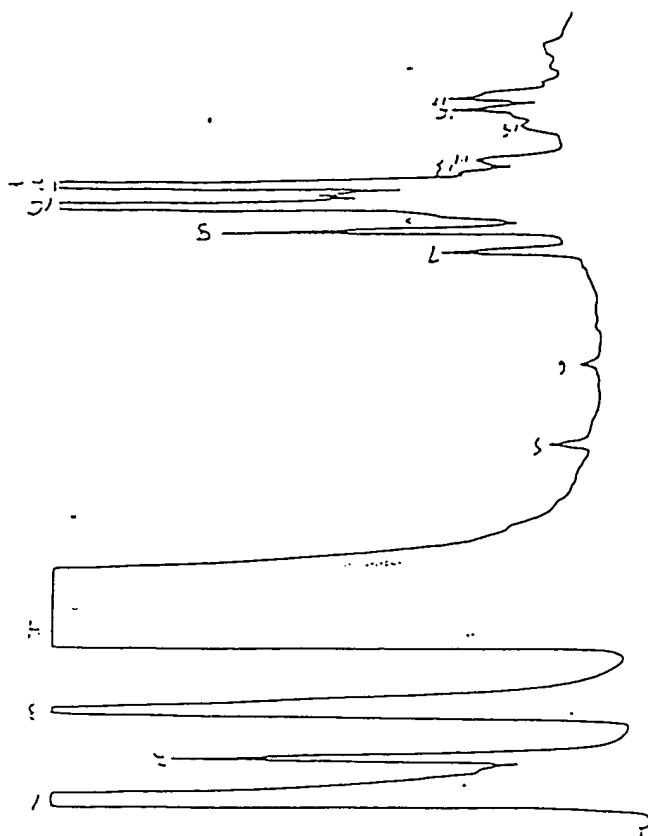


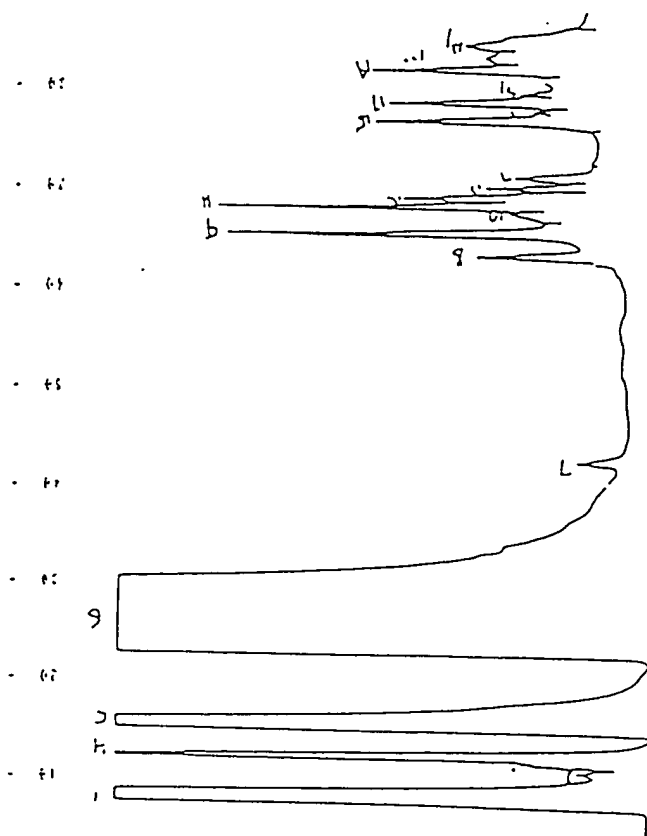
FIG 28B: ALKYLATED

* Lys-C digests of
TNF- α

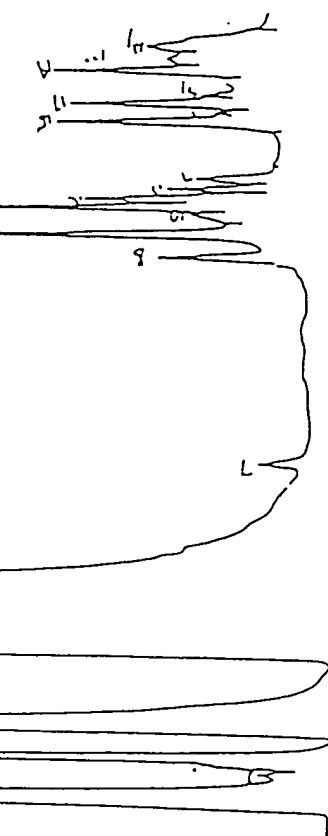
re-chromatograph
evens 15, 21, 25, 28, 32, 34



re-chromatograph
odds 13, 25, 27, 33, 37

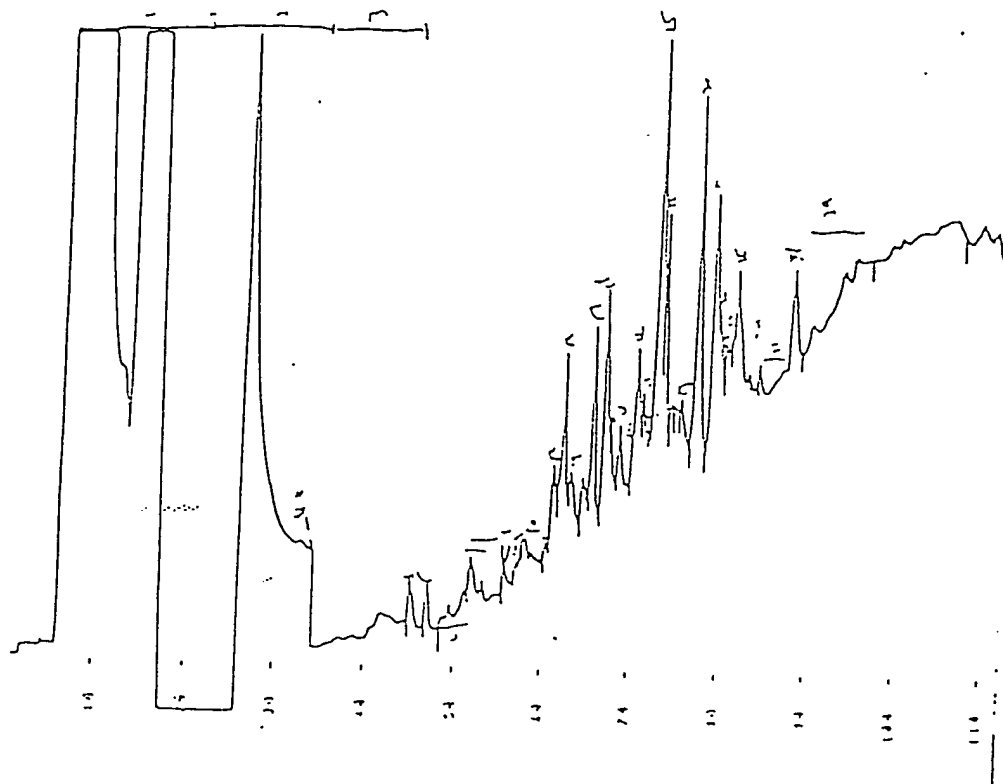


re-chromatograph
odds 13, 25, 27, 33, 37

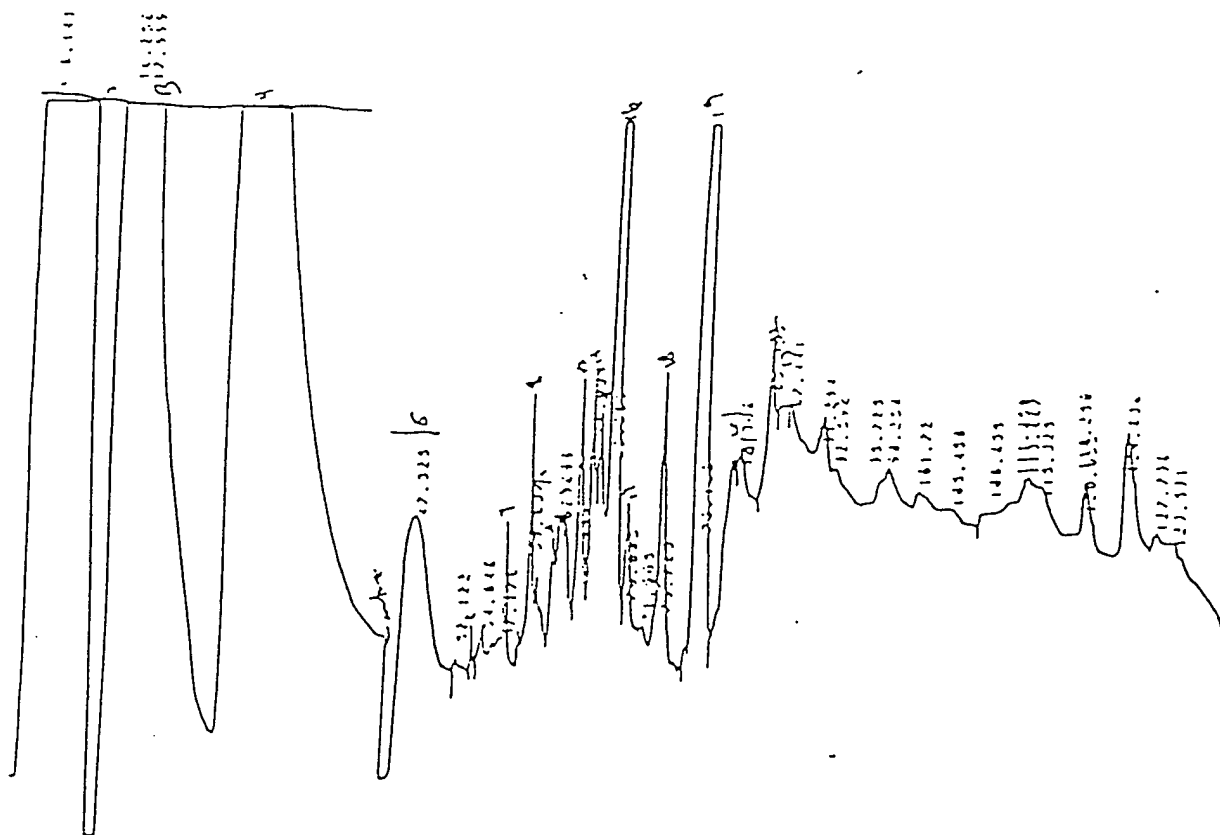


F-6. 29

#1



#2



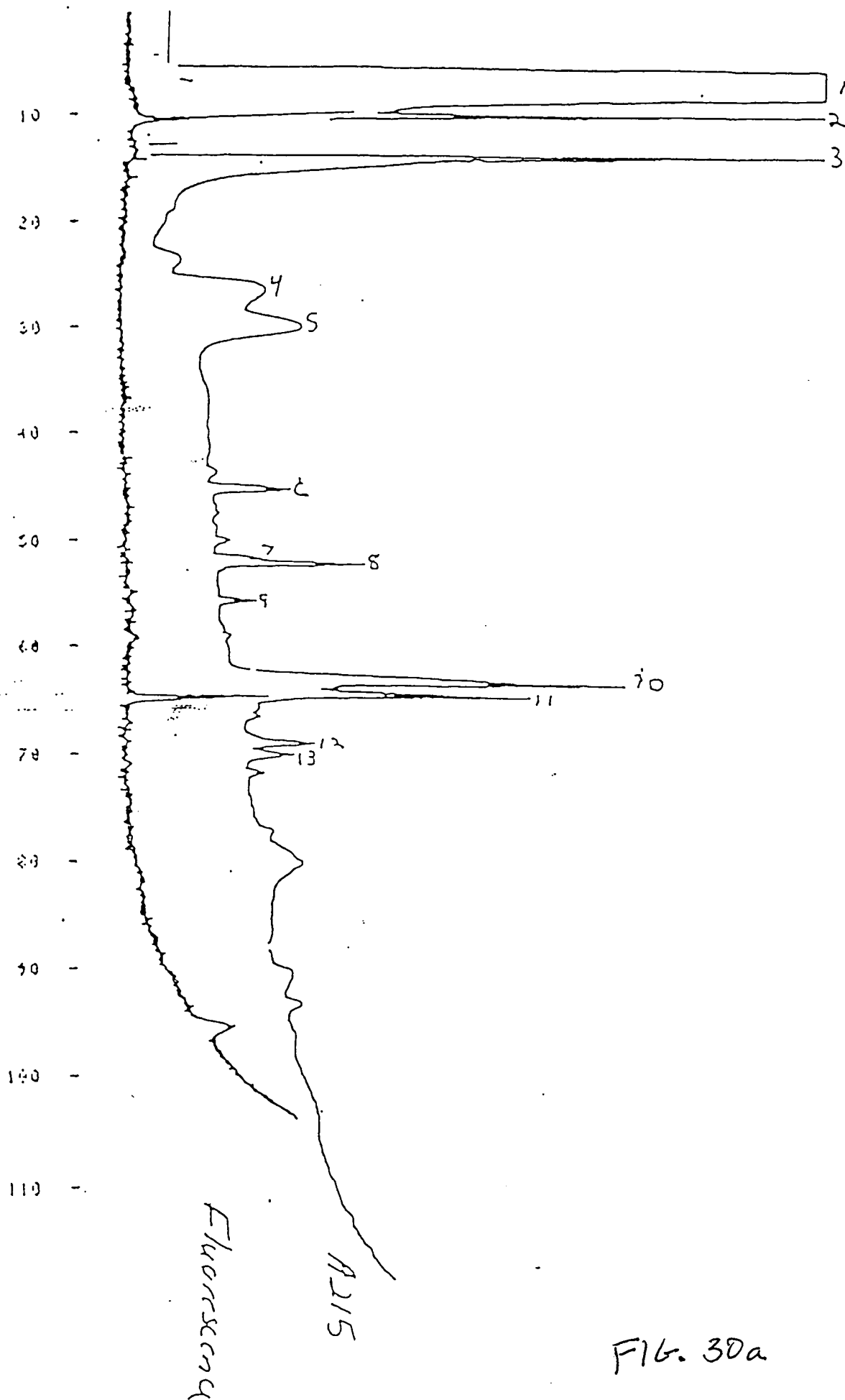
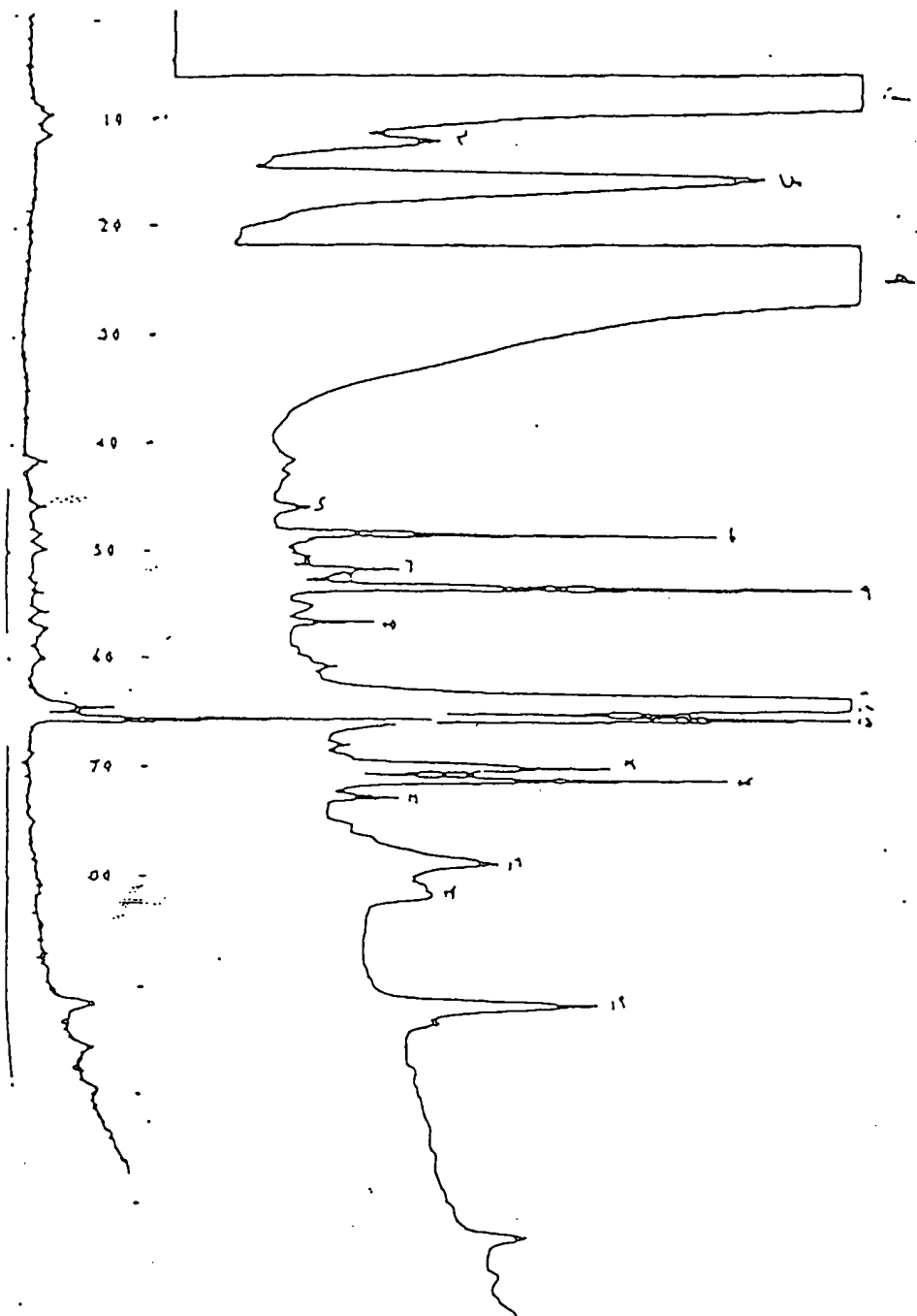


FIG. 30a

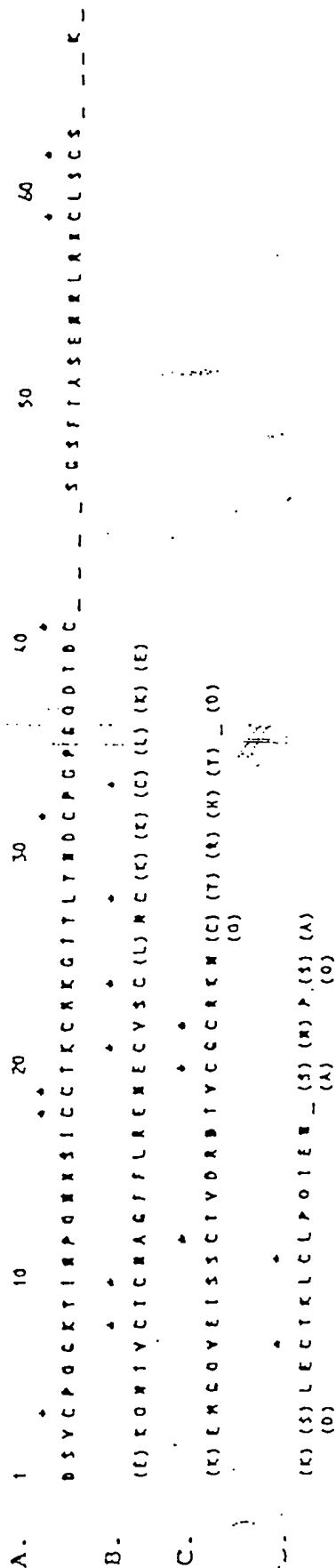
F16. 30/3



A215

Fluorescence

Figure 31



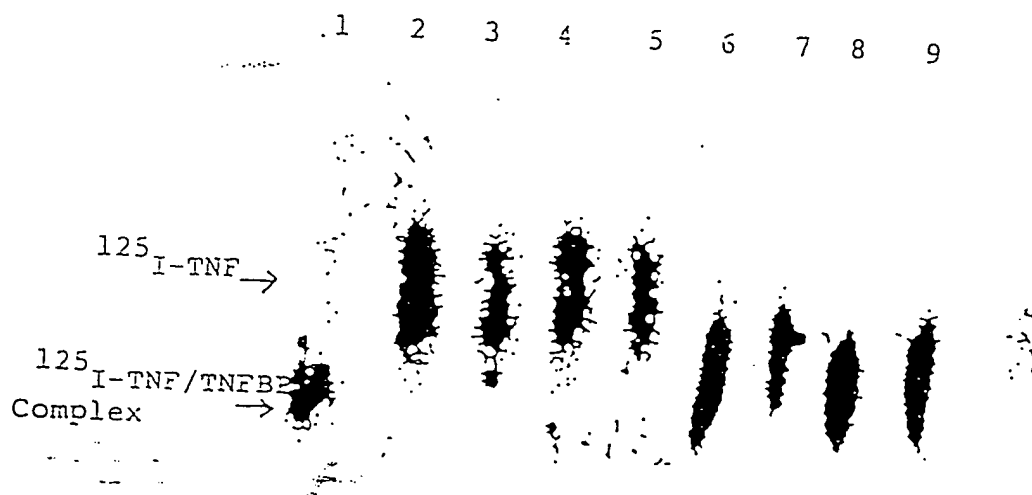
20 30 40 50 60 70
 CATGCCGCA GGTGGACTCT AGAGGATCTG GGUCCCTACTA GCTTTGAGTT GAGUGAACAA AAATGAAAC
 80 90 100 110 120 130 140
 ACAGGACAAAC TAGAGAACAA TTAAGCATER GATTGTATGC CCCAACTGTC TAAGTTTCAA GGAAGAACTC
 150 160 170 180 190 200 210
 TAAACTTAGT GAGTGGCCTG GCCTGGGCGG AATGTTTCAC TGAGGAAGGA CTTGAUCCAG GGAAGTTTAA
 220 230 240 250 260 270 280
 GATCTGCTAC CCCTAAGCTT CCCATCCCTC CCTCTCTTGA TGGTGTCTCC TCTATCTGAT TCTTCCCCAG
 289 298 307 316 325 334
 GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CTC TCA GGG GTT ATT GGA CTG GTC
 Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu Val
 343 352 361 370 379 388
 CCT CAC CTA GGG GAC AGG GAG AGC AGA GAT AGT GTG TGT CCC CAA GCA AAA TAT
 Pro His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln Gly Lys Tyr
 397 406 415 424 433 442
 ATC CAC CCT CAA AAT AAT TCG ATT TCG TGT ACC AAG TCC CAC AAA G GTAUGGGCAA
 Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys Ala
 451 460 469 478 487 496 505 514
 GTUGAAACGG TGAATGCCCT CAGGTCTAGG GTUCIGCTTC TTTCTCTGCT TCTTCCAGTT GTTCTTCCCT
 524 534 544 554 564 574 584
 AACTTTGCTG TCTCTCTGCG GUTGAGATT TCTCCCTCCC TCTCTCTCTA GAGACTTCAG GGAATCGGCC
 594 604 614 624 634 644 654
 CTGGGCTGTTG TCCTTAGCAT GGGGCTCCTT CTTGTGTGTC TCACCCSCAG CCTAACTCTG CCGGCCCCATT
 664 673 682 691 700
 CA CA GAA ACC TAC TTG TAC AAT GAC TGT CCA GGC CCG GGG CAG GAT ACC GAC
 Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Arg
 709 718 727 736 745 754
 TGC AGG GAG TGT GAG AGC GGC TCC TTC ACC GCT TCA GAA AAC CAC CTC AGA CAC
 Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His
 763 772 781 790 800 810
 TGC CTC AGC TGC TCC AAA TGC CGA AAG GGTGAGTGTG CACAGGCAGG AGAGTCAGGC
 Cys Leu Ser Cys Ser Lys Cys Arg Lys
 827 837 847 857 867 877 887
 GGGTCTTCAAG TGGTGTGTGG GTCCCTGTCT ATGTGCAGGC TGGTGGGTGT GGGCAGGAGG GTGTGTGTGT
 897 907 917 927 937 947 957
 TGTGTCGACA CTGATGGAT GTGAGTGTGT ATTACAGAGA CACACACTTA GGGGTATGTC AGTAAGGCTA
 967 977 987 997 1007 1016
 TGCAGGAGAA GGAGGATGCA GAACTCATAC CCCATCTTCT CCCCACCA GAA ATG GAT CAG
 Glu Met Gly Gln
 1025
 GTG GAT ATC
 Val Glu Ile

F/G. 33

1 10 20 30 40 50 60 70 80
D S Y C P O G K T I X P O X M S I C C T K C M K G T Y L Y W D C P G P G O D T D C A E C E S G S F T A S E X H L A X C L S C S K C R K E M G Q V E I S S C T V D R D T
Y C C C R K X

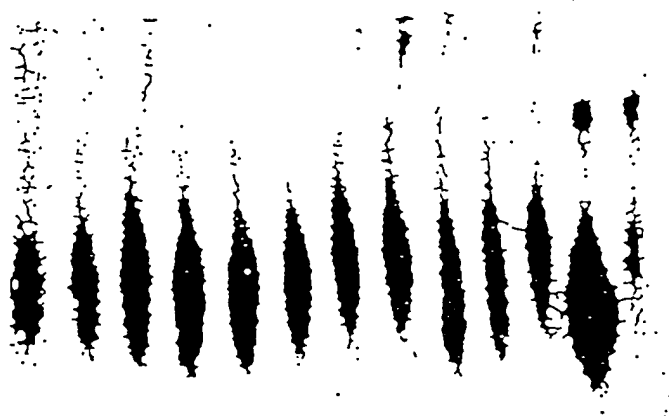
K O M T V C T E H A G T F L R E X E C V S C

L E C T K L C L P O I E X



Lane 1 is a positive control. Purified TNF-BP complexed with ^{125}I -TNF. Lane 2-5 are protein from the 24, 48, 72, and 96 hour incubations with PMA/PHA that did not bind to the TNF-affinity column. Lane 6-9 are the material from the same incubations that did bind to the TNF-affinity column.

25 26 27 28 29 30 31 32 33 34 35 + -



Fractions 27, 28 and 29, 33 and 34 show TNF binding activity. + is as lane 1 of figure 15. - is ^{125}I -TNF alone.

NO	PMA/PHA	
	1 hr	17 hr
PMA/PHA		

9.49 Kb
7.46
4.4
2.3
1.3

Fig 36

11 21 51 12 22 52



FIG 37

10 20
 Asp Ser Val Cys Pro Gln Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr
 30 40
 Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp
 50 60
 Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu
 70 80
 Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val Glu Ile Ser Ser Cys Thr Val Asp
 90 100
 Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu
 110 120
 Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu
 130 140
 Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu Asn Glu Cys Val
 150 160
 Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr Lys Leu Cys Leu Pro Gln Ile Glu
 161
 Asn

FIG 38

296 305

GAT AGT GTG TGT CCC CAA
Asp Ser Val Cys Pro Gln

314 323 332 341 350 359

GGA AAA TAT ATC CAC CCT CAA AAT AAT TCG ATT TGC TGT ACC AAG TGC CAC AAA
Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys

368 377 386 395 404 413

GGA ACC TAC TTG TAC AAT GAC TGT CCA GGC CCG GGG CAG GAT ACG GAC TGC AGG
Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp Cys Arg

422 431 440 449 458 467

GAG TGT GAG AGC GGC TCC TTC ACC GCT TCA GAA AAC CAC CTC AGA CAC TGC CTC
Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu

476 485 494 503 512 521

AGC TGC TCC AAA TGC CGA AAG GAA ATG GGT CAG GTG GAG ATC TCT TCT TGC ACA
Ser Cys Ser Lys Cys Arg Lys Glu MET Gly Gln Val Glu Ile Ser Ser Cys Thr

530 539 548 557 566 575

GTG GAC CGG GAC ACC GTG TGT GGC TGC AGG AAG AAC CAG TAC CGG CAT TAT TGG
Val Asp Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp

584 593 602 611 620 629

AGT GAA AAC CTT TTC CAG TGC TTC AAT TGC AGC CTC TGC CTC AAT GGG ACC GTG
Ser Glu Asn Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val

638 647 656 665 674 683

CAC CTC TCC TGC CAG GAG AAA CAG AAC ACC GTG TGC ACC TGC CAT GCA GGT TTC
His Leu Ser Cys Gln Glu Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe

692 701 710 719 728 737

TTT CTA AGA GAA AAC GAG TGT GTC TCC TGT AGT AAC TGT AAG AAA AGC CTG GAG
Phe Leu Arg Glu Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu

746 755 764

TGC ACG AAG TTG TGC CTA CCC CAG ATT GAG AAT
Cys Thr Lys Leu Cys Leu Pro Gln Ile Glu Asn

Figure 39

10	20	30	40	50	60	70
GATCACTSGG ACCAGGCCGT GATCTCTATG CCCGAGTCTC AACCTCAAC TGTCACCCCA AGGCACTTGG						
80	90	100	110	120	130	140
GACGTCCTGG ACAGACCGAG TCCCGGGAAG CCCAGCACT GCCGCTGCCA CACTGCCCTG AGCCCAAATG						
150	160	171	180	189	198	
GGGGAGTGAG AGGCCATAGC TGTCTGGC ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG						
MET Gly Leu Ser Thr Val Pro Asp Leu Leu						
207	216	225	234	243	252	
CTG CCG CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT						
Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile						
261	270	279	288	297	306	
GGA CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA SAT AGT GTG TGT CCC CAA						
Gly Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln						
315	324	333	342	351	360	
GSA AAA TAT ATC CAC CCT CAA AAT AAT TCG ATT TGC TGT ACC AAG TGC CAC AAA						
Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys						
369	378	387	396	405	414	
GGA ACC TAC TTG TAC AAT GAC TGT CCA GGC CCG GGG CAG GAT ACG GAC TGC AGG						
Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp Cys Arg						
423	432	441	450	459	468	
GAG TGT GAG ASC GGC TCC TTC ACC GCT TCA GAA AAC CAC CTC AGA CAC TGC CTC						
Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu						
477	486	495	504	513	522	
AGC TGC TCC AAA TGC CGA AAG GAA ATG GGT CAG GTG GAG ATC TCT TCT TGC ACA						
Ser Cys Ser Lys Cys Arg Lys Glu MET Gly Gln Val Glu Ile Ser Ser Cys Thr						
531	540	549	558	567	576	
GTG GAC CCG GAC ACC GTG TGT GGC TGC AGG AAG AAC CAG TAC CCG CAT TAT TGG						
Val Asp Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp						
585	594	603	612	621	630	
AGT GAA AAC CTT TTC CAG TGC TTC AAT TGC AGC CTC TGC CTC AAT GGG ACC GTG						
Ser Glu Asn Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val						
639	648	657	666	675	684	
CAC CTC TCC TGC CAG GAG AAA CAG AAC ACC GTG TGC ACC TGC CAT GCA GGT TTC						
His Leu Ser Cys Gln Glu Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe						

693	702	711	720	729	738
TTT CTA AGA GAA AAC GAG TGT GTC TCC TGT AGT AAC TGT AAG AAA AGC CTG GAG Phe Leu Arg Glu Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu					
747	756	765	774	783	792
TGC ACG AAG TTG TGC CTA CCC CAG ATT GAG AAT GTT AAG GGC ACT GAG GAC TCA Cys Thr Lys Leu Cys Leu Pro Gln Ile Glu Asn Val Lys Gly Thr Glu Asp Ser					
801	810	819	828	837	846
GGC ACC ACA GTG CTG TTG CCC CTG GTC ATT TTC TTT GGT CTT TGC CTT TTA TCC Gly Thr Thr Val Leu Leu Pro Leu Val Ile Phe Phe Gly Leu Cys Leu Leu Ser					
855	864	873	882	891	900
CTC CTC TTC ATT GGT TTA ATG TAT CGC TAC CAA CCG TGG AAG TCC AAG CTC TAC Leu Leu Phe Ile Gly Leu MET Tyr Arg Tyr Gln Arg Trp Lys Ser Lys Leu Tyr					
909	918	927	936	945	954
TCC ATT GTT TGT GGG AAA TCG ACA CCT GAA AAA GAG GGG GAG CTT GAA GGA ACT Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys Glu Gly Glu Leu Glu Gly Thr					
963	972	981	990	999	1008
ACT ACT AAG CCC CTG GCC CCA AAC CCA AGC TTC AGT CCC ACT CCA GGC TTC ACC Thr Thr Lys Pro Leu Ala Pro Asn Pro Ser Phe Ser Pro Thr Pro Gly Phe Thr					
1017	1026	1035	1044	1053	1062
CCC ACC CTG GGC TTC AGT CCC GTG CCC AGT TCC ACC TTC ACC TCC AGC TCC ACC Pro Thr Leu Gly Phe Ser Pro Val Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr					
1071	1080	1089	1098	1107	1116
TAT ACC CCC GGT GAC TGT CCC AAC TTT GCG GCT CCC CGC AGA GAG GTG GCA CCA Tyr Thr Pro Gly Asp Cys Pro Asn Phe Ala Ala Pro Arg Arg Glu Val Ala Pro					
1125	1134	1143	1152	1161	1170
CCC TAT CAG GGG GCT GAC CCC ATC CTT GCG ACA GCC CTC GCC TCC GAC CCC ATC Pro Tyr Gln Gly Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala Ser Asp Pro Ile					
1179	1188	1197	1206	1215	1224
CCC AAC CCC CTT CAG AAG TGG GAG GAC AGC SCC CAC AAG CCA CAG AGC CTA GAC Pro Asn Pro Leu Gln Lys Trp Glu Asp Ser Ala His Lys Pro Gln Ser Leu Asp					
1233	1242	1251	1260	1269	1278
ACT GAT GAC CCC GCG ACG CTG TAC GCC GTG GTG GAG AAC GTG CCC CCG TTG CGC Thr Asp Asp Pro Ala Thr Leu Tyr Ala Val Val Glu Asn Val Pro Pro Leu Arg					
1287	1296	1305	1314	1323	1332
TGG AAG GAA TTC GTG CGG CGC CTA GGG CTG AGC GAC CAC GAG ATC GAT CGG CTG Trp Lys Glu Phe Val Arg Arg Leu Gly Leu Ser Asp His Glu Ile Asp Arg Leu					

1341	1350	1359	1368	1377	1386
SAG CTG CAG AAC GGG CGC TGC CTG CGC GAG GCG CAA TAC AGC ATG CTG GCG ACC					
Glu Leu Gln Asn Gly Arg Cys Leu Arg Glu Ala Gln Tyr Ser MET Leu Ala Thr					
1395	1404	1413	1422	1431	1440
TGG AGG CCG CGC ACG CCG CCG CGC GAG GCC ACG CTG GAG CTG CTG GGA CGC GTG					
Trp Arg Arg Arg Thr Pro Arg Arg Glu Ala Thr Leu Glu Leu Leu Gly Arg Val					
1449	1458	1467	1476	1485	1494
CTC CGC GAC ATG GAC CTG CTG GGC TGC CTG GAG GAC ATC GAG GAG GCG CTT TGC					
Leu Arg Asp MET Asp Leu Leu Gly Cys Leu Glu Asp Ile Glu Glu Ala Leu Cys					
1503	1512	1521	1530	1546	1556
GGC CCC GCC GCC CTC CCG CCC GCG CCC AGT CTT CTC AGA TGA					
Gly Pro Ala Ala Leu Pro Pro Ala Pro Ser Leu Leu Arg					
1566	1576	1586	1596	1606	1626
CTCTAAGGAC CGTCCTGCGA GATCGCCTTC CAACCCCACT TTTTCTGGA AAGGAGGGGT CCTGCAGGGG					
1636	1646	1656	1666	1676	1686
CAAGCAGGAG CTAGCAGCCG CCTACTTGGT GCTAACCCCT CGATGTACAT AGCTTTTCTC AGCTGCCTGC					
1706	1716	1726	1736	1746	1766
GCSCCGCCGA CAGTCAGCGC TGTGCGCGCG GAGAGAGGTG CGCCGTGGGC TCAAGAGCCT GAGTGGGTGG					
1776	1786	1796	1806	1816	1836
TTTGCGAGGA TGAGGGACGC TATGCCTCAT GCCCGTTTTG GGTGTCTCA CCAGCAAGGC TGCTCGGGGG					
1846	1856	1866	1876	1886	1906
CCCCTGGTTC GTCCTGAGC CTTTTTCACA GTGCATAAGC AGTTTTTTTT GTTTTTGTTT TGTTTTGTTT					
1916	1926	1936	1946	1956	1976
TGTTTTTAAA TCAATCATGT TACACTAATA GAACTTGGC ACTCCTGTGC CCTCTGCCTG GACAAGCACA					
1986	1996	2006	2016	2026	2046
TAGCAAGCTG AACTGTCCTA AAGCAGGGGC GAGCACGSA CAATGGGGCC TTCAGCTGGA GCTGTGGACT					
2056	2066	2076	2086		
TTTGTACATA CACTAAAATT CTGAAGTTAA ASCTCAAAAA AA					

Fig. 41

GA ATT CCA CAA CGG TTT CCC TCT AGA AAT AAT TTT GTT TAA CTT TAA GAA GGA GAT ATA CAT

Start gene 10 protein sequence

ATG GCT AGC ATG ACT GGT CGA CAG CAA ATG GGT ACG GAT CCG ATC TTG GAG GAT GAT TAA
 Met Ala Ser Met Thr Gly Gln Gln Met Gly Thr Asp Pro Ile Leu Glu Asp Asp Stop
 Translational coupler

ATG GAC AGC GTT TGC CCC
 Met Asp Ser Val Cys Pro
 Start TNF inhibitor sequence

Fig. 23

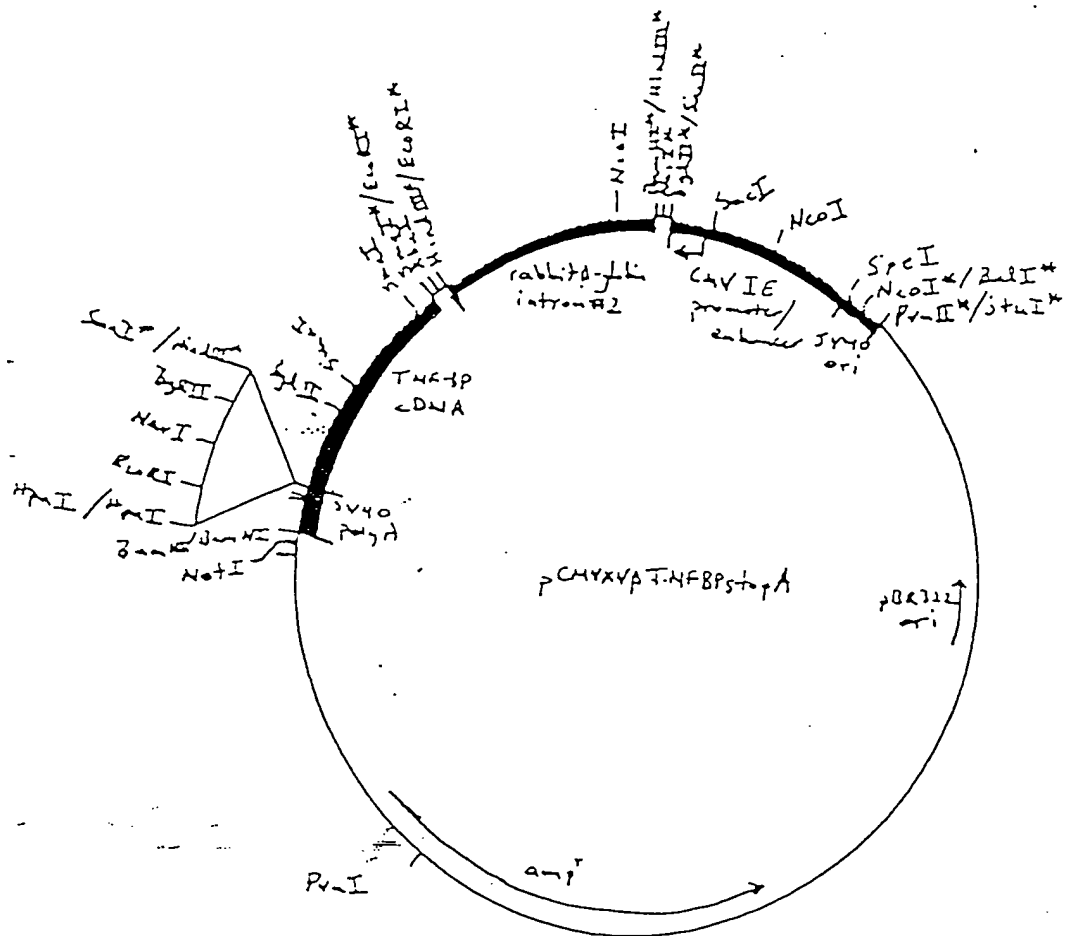
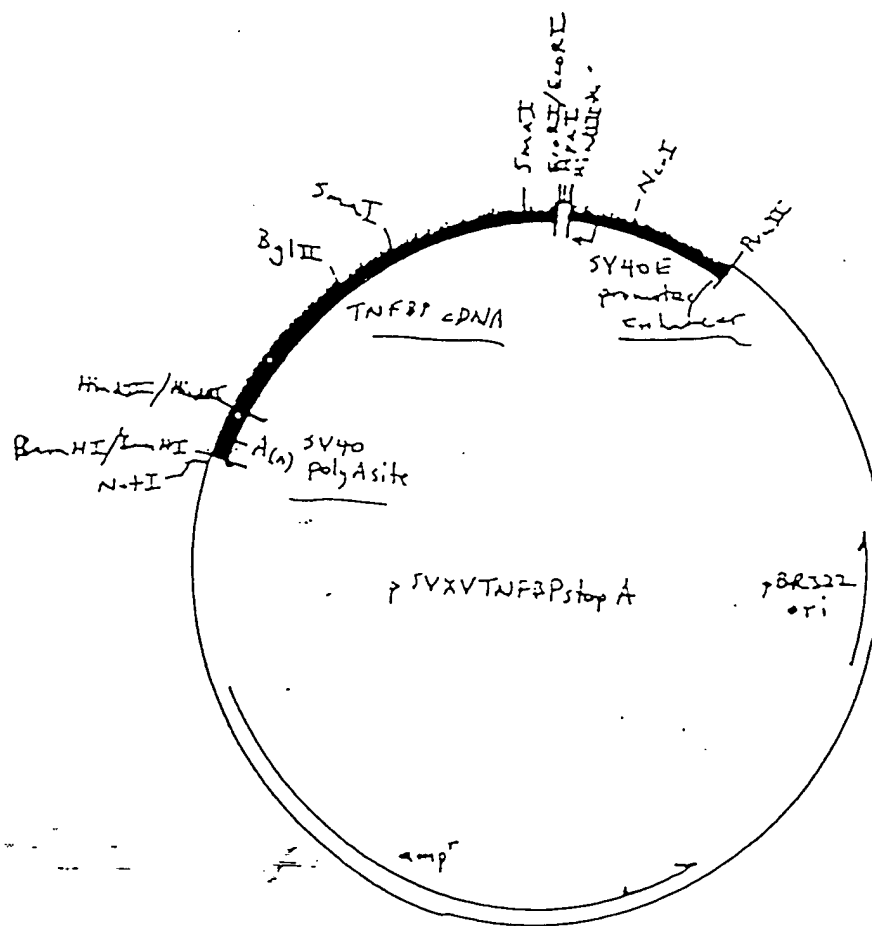


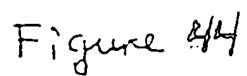
FIG. 42

Fig. 24



* - restriction site no longer exists:

FIG. 43



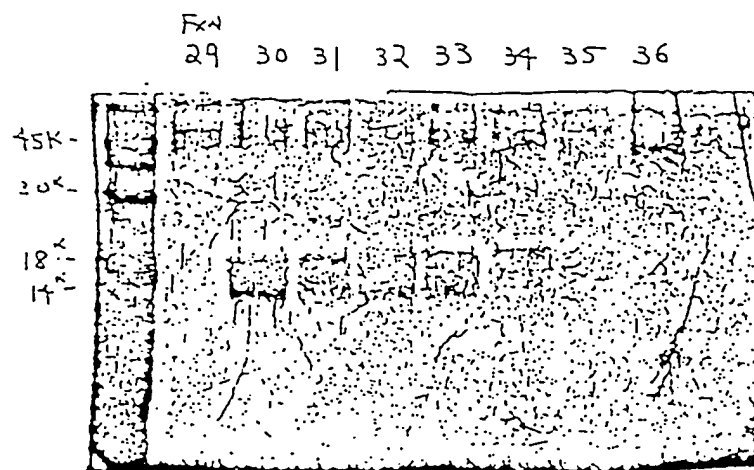


Figure 45

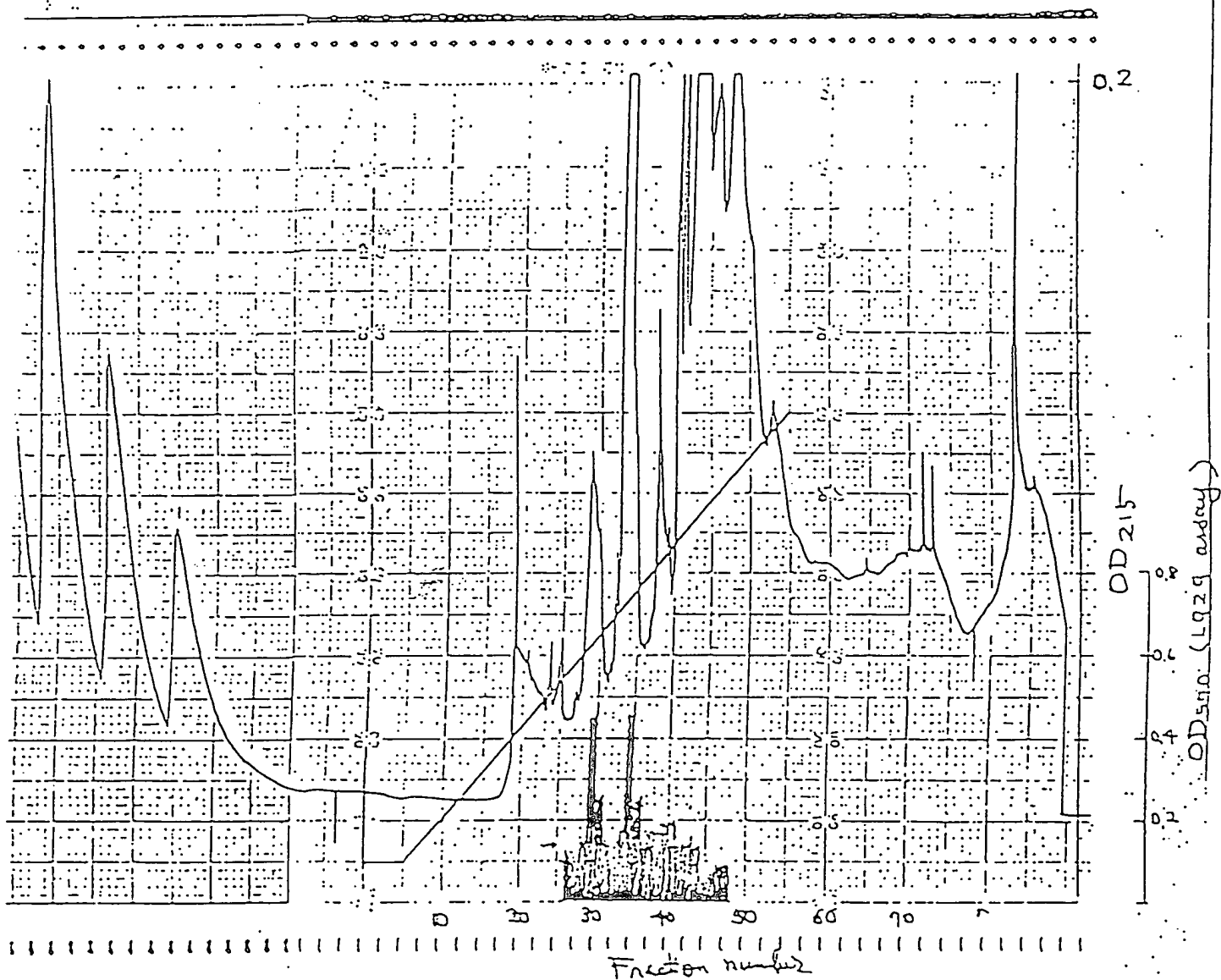


Fig. 46

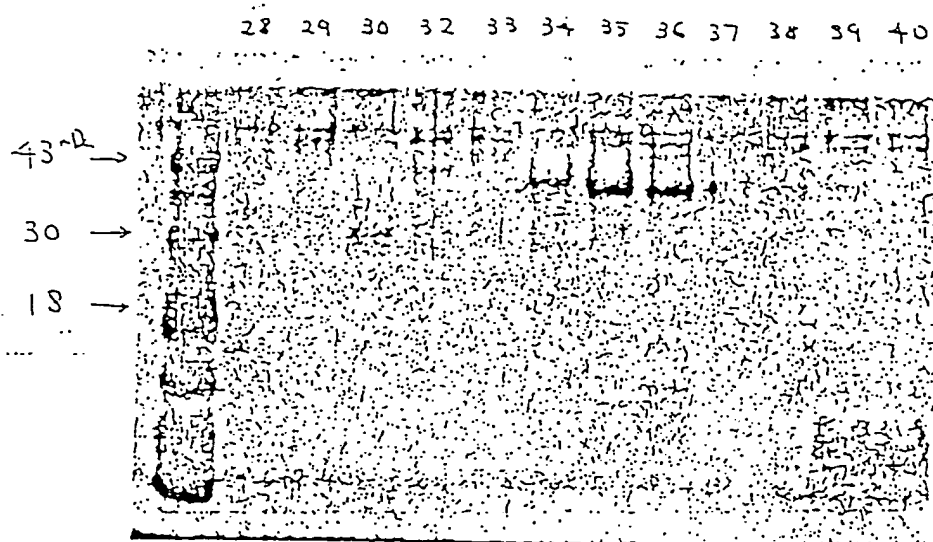
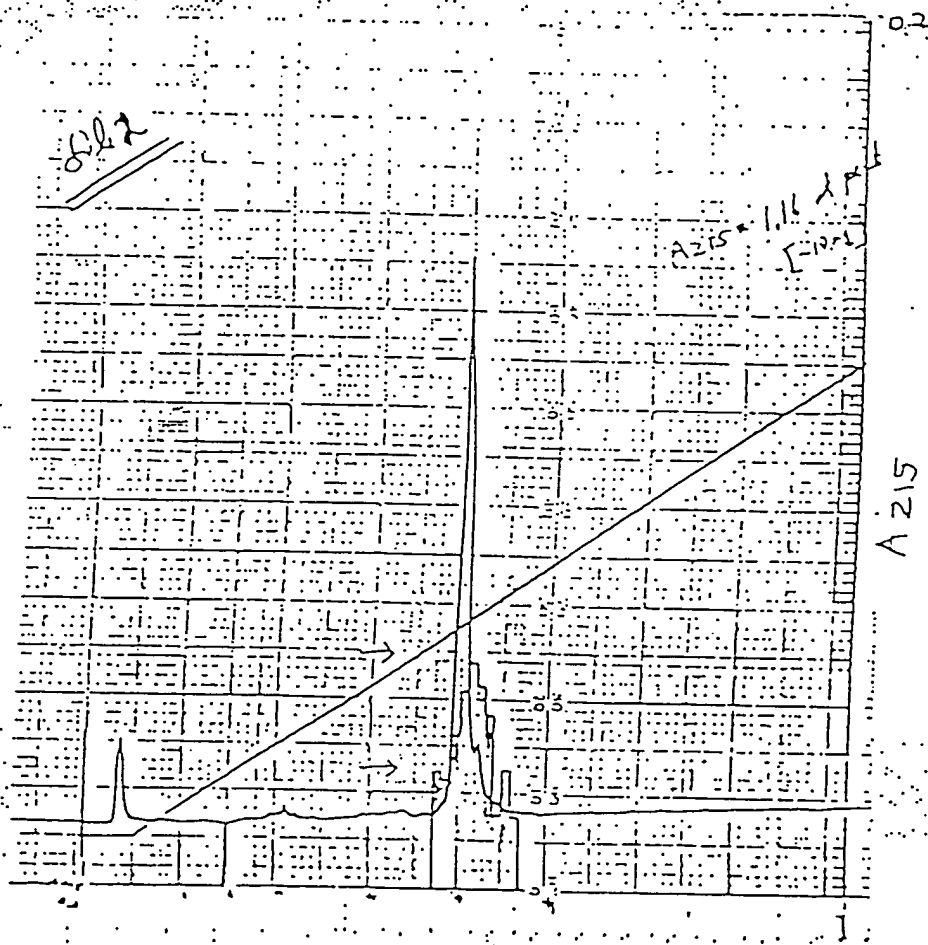


Fig. 47



34 33 32 31 30 29



← 43 kDa

← 30 kDa

← 18 kDa

Fig. 50

U937-derived TNF-INH1 (30 kDa)

()-()-Val-()-Pro-Gln-GLY-Lys-Tyr-Ile-His-Pro-Gln-
()-Asn-()-Ile

U939-derived TNF-INH2 (40 kDa)

Leu-Pro-Ala-Gln-Val-Ala-Phe-Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-
Ser-Thr-Cys-Arg-Leu-Arg-Glu-Tyr-Tyr-Asp-Gln-Thr-Ala-Gln-Met-
Cys-Cys-Ser-Lys-Cys-

Urine-derived TNF-INH2 (40 kDa)

Ala-Gln-Val-Ala-Phe-Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr-
Cys-()-Leu-()-Glu

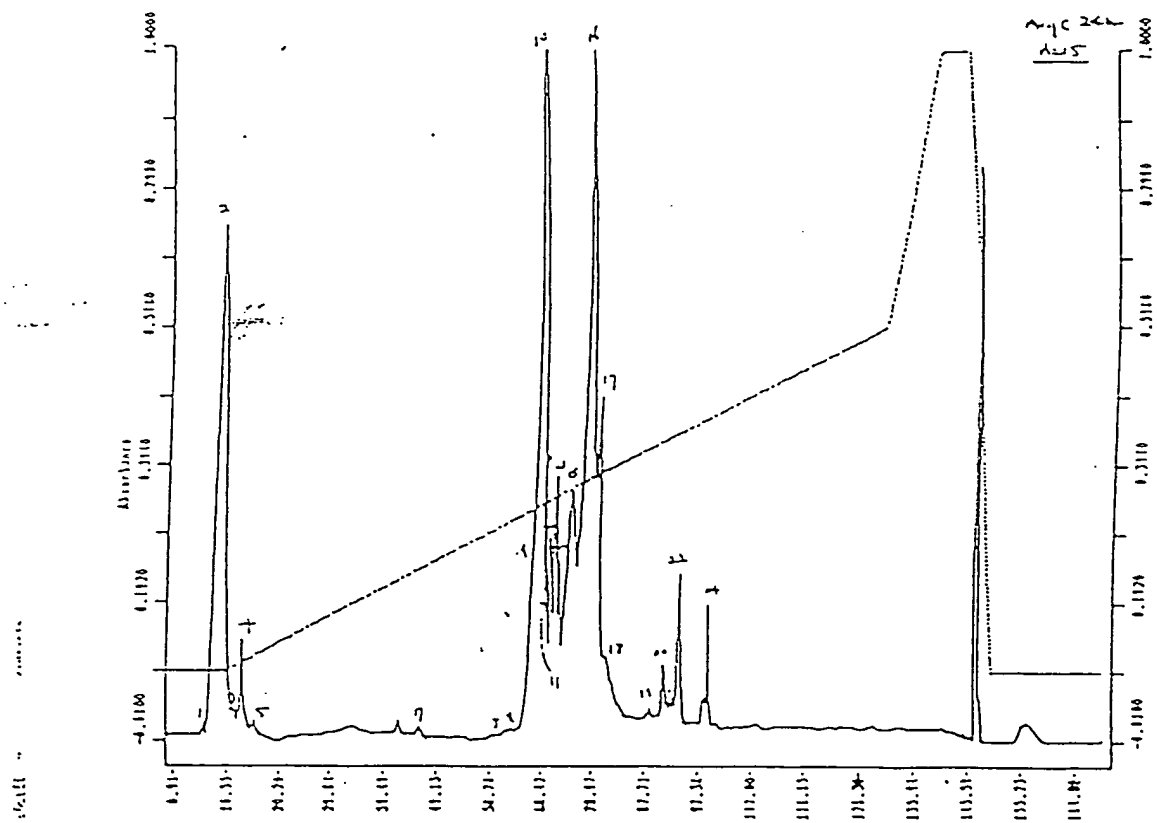


Figure 52

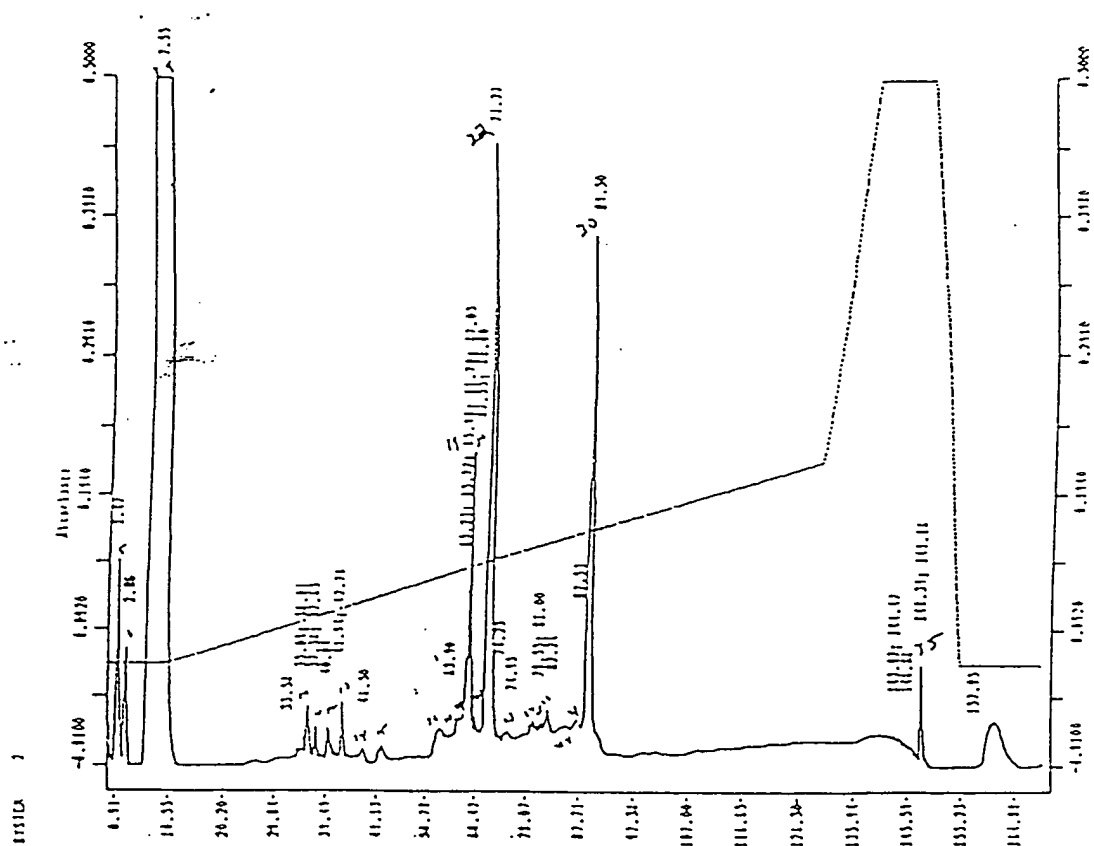


Fig. 53

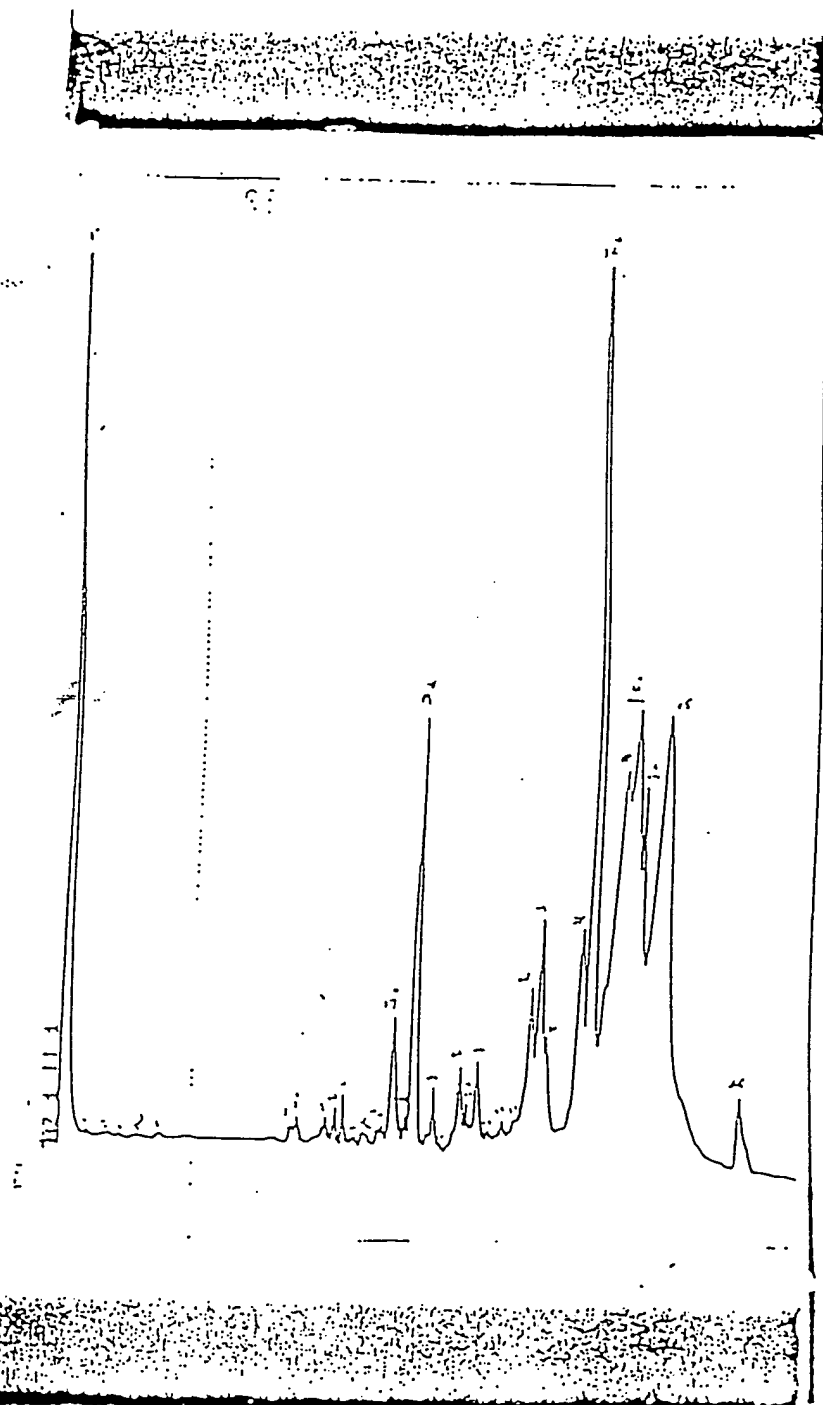


Figure 56

5' - CCG
Pro

58	64	73	82	91	100
GAG CCC GCG AGC ACA TGC CGG CTC AGA GAA TAC TAT GAC CAG ACR GCH CAR ATG Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln MET					
109	118	127	136	145	154
TGC TGC AGC AAG TGC TCG CCG GGC CAA CAT GCA AAA GTC TTC TGT ACC AAG ACC Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr					
163	172	181	190	199	208
TCC GAC ACC GTG TGT GAC TCC TGT GAG GAC AEC ACA TAC ACC CAG CTC TGG AAC Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn					
217	226	235	244	253	262
TGG GTT CCC GAG TGC TTG AGC TGT GGC TCC CGC TGT AGC TCT GAC CAG GTG GAA Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln Val Glu					
271	280	289	298	307	316
ACT CAA GCC TGC ACT CGG GAA CAG AAC LGC ATC TGC ACC TGC AAG CCC GGC TGG Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp					

325

TAY TGC - 3'
Tyr Cys

Figure 57

Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser
Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln MET Cys Cys
Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr
Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu
Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser
Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys
Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys
Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala
Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro
Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His
Gln Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Arg Asp Ala
Val Cys Thr Ser Thr Ser Pro Thr Arg Ser MET Ala Pro Gly Ala Val
His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr
Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro MET Gly
Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp

60	90	101	110	119
CAACCGGACC CCGCCCGCAC CC	ATG GCG CCC GTC GCG GTC TGG GCG GCG CTG GCC			
	MET Ala Pro Val Ala Val Trp Ala Ala Leu Ala			
128	137	146	155	164
GTC GGA CTG GAG CTC TGG GCT GCG GCG CAC GCG TTG CCC GCG CAG GTG GCA TTT				
Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe				
182	191	200	209	218
ACA CCC TAC GCG CCG GAG CCC GCG AGC ACA TGC CCG CTC AGA GAA TAC TAT GAC				
Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp				
236	245	254	263	272
CAG ACA GCT CAG ATG TGC TGC AGC AAU TGC TCG CCG GCG CAA CAT GCA AAA GTC				
Gln Thr Ala Gln MET Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val				
290	299	308	317	326
TTC TGT ACC AAG ACC TCG GAC ACC GTG TGT GAC TCC TGT GAG GAC AGC ACA TAC				
Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr				
344	353	362	371	380
ACC CAG CTC TCG AAC TGG GTT CCC GAG TGC TTG AGC TGT GCG TCC CCG TGT AGC				
Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser				
398	407	416	425	434
TCT GAC CAG GTG GAA ACT CAA GCC TGC ACT CCG GAA CAG AAC CCG ATC TCG ACC				
Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr				
452	461	470	479	488
TGC AGC CCC GCG TCG TAC TGC GCG CTG AGC AAG CAG GAG GCG TGC CGG CTG TGC				
Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu Cys				
506	515	524	533	542
GCG CCG CTG CCG AAG TGC CCG CCG GCG TTC GCG GTG GCG AGA CCA GGA ACT GAA				
Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu				
560	569	578	587	596
ACA TCA GAC GCG GTG TGC AAG CCC TGT GCG CCG GCG ACG TTC TCC AAC ACG ACT				
Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr				
614	623	632	641	650
TCA TCC ACG GAT ATT TGC ACG CCC CAC CAG ATC TGT AAC GTG GTG GCG ATC CCT				
Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro				
668	677	686	695	704
GCG AAT GCA AGC AGG GAT GCA GTC TGC ACG TCC ACG TCC CCG ACC CCG AGT ATG				
Gly Asn Ala Ser Arg Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser MET				
722	731	740	749	758
GCC CCA GCG GCA GTA CAC TTA CCC CAG CCA GTG TCC ACA CCA TCC CAA CAC ACG				
Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr				
776	785	794	803	812
CAG CCA ACT CCA GAA CCC AGC ACT GCT CCA AGC ACC TCC TTC CTG CTC CCA ATG				
Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro MET				
830	839	848	857	866
GCG CCG AGC CCC CCA GCT GAA GCG AGC ACT GCG GAC TTC GCT CTT CCA GTT GGA				
Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly				
884	893	902	911	920
CTG ATT GTG GGT GTG ACA GCC TTG GGT CTA CTA ATA ATA GGA GTG GTG AAC TGT				
Leu Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn Cys				
938	947	956	965	974
GTC ATC ATG ACC CAG GTG AAA AAG AAG CCC TTG TGC CTG CAG AGA GAA GCC AAG				
Val Ile MET Thr Gln Val Lys Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys				
992	1001	1010	1019	1028
GTA CCA CAC TTG CCA GCG GAT AAG GCG GCG GGT ACA CAG ACC CCC GAG CAG CAG				
Val Pro His Leu Pro His Asp Lys His Arg Gly Thr Gln Gly Pro Glu Gln Gln				

Figure
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1046 1064 1073 1082
 CAC CTG CTG CCA GCG CCG AGC TCC AGC AGC TCC CTG TCC GCG
 His Leu Leu Thr Ala Pro Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala
 1100 1109 1118 1127 1136 1143
 AGT GCG TTG GAC AGA AGG GCG CCC ACT CGG AAC CAG CCA CAG GCA CCA GGC GTG
 Ser Ala Leu Asp Arg Arg Ala Pro Thr Arg Arg Gln Pro Gln Ala Pro Gly Val
 1154 1163 1172 1181 1190 1199
 GAG GCG AGT GGG GCG GGG GAG GCG CGG GCG AGC ACC GGG AGC TCA GAT TCT TCC
 Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser
 1208 1217 1226 1235 1244 1253
 CCT GGT GGC CAT GGG ACC CAG GTC AAT GTC ACC TGC ATC GTG AAC GTC TGT AGC
 Pro Gly Gly His Gly Thr Gln Val Arg Val Thr Cys Ile Val Arg Val Cys Ser
 1262 1271 1280 1289 1298 1307
 AGC TCT GAC CAC AGC TCA CAG TGC TCC TCC CAA GCG AGC TCC ACA ATG GGA GAC
 Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln Ala Ser Ser Thr Met Gly Asp
 1316 1325 1334 1343 1352 1361
 ACA GAT TCC AGC CCC TCG GAG TCC CCG AAG GAC GAG CAG GTC CCC TTC TCC AAG
 Thr Asp Ser Ser Pro Ser Glu Ser Pro Lys Asp Glu Gln Val Pro Phe Ser Lys
 1370 1379 1388 1397 1406 1415
 GAG GAA TGT GGC TTT GGG TCA CAG CTG GAG ACC CCA GAG ACC CTG CTG GGG AGC
 Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser
 1424 1433 1442 1451 1460 1469
 ACC GAA GAG AAG CCC CTG CCC CTT GGA GTG CCT GAT GCT GAG ATG AAG CCC AGT
 Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser
 1478 1488 1498 1508 1518 1528 1530
 TAA CCAAGCCGGT GTGGGCTGTG TCGTAGCCAA GGTGGGCTGA GCCCTGGGAG GATGACCCGT
 1542 1558 1568 1578 1588 1598 1608
 CCAAGGGGCG CTGGTCTTC CAGGCCCCCA CCACTAGGAC TCTGAGGCTC TTCTGAGCC AATCTCTCT
 1618 1628 1638 1648 1658 1668 1678
 AGTGGCTCC AAGGCGCAG CTECTCTCTG ACCTGCAGGC CAGGAGCAGA GGCAGCGGT TGTGGAAGC
 1688 1698 1708 1718 1728 1738 1748
 CTCTGCTGCC ATGCTGTGTC CCTCTCGAA GGTGAGCTG GATGAGGCT TCGGGGCTG CTGGGAGAG
 1758 1768 1778 1788 1798 1808 1818
 TCCCTGACTC TCTGTGACT GCCCGGCCCA GCTGCACTG CCAAGCTGAC TTCTGAGGCC CTGAGTTTT
 1828 1838 1848 1858 1868 1878 1888
 TTGTTTGTG GTTGTGTTG TTGTTTGTG CTCCCTCTG GCTCTGCCCC AGCTCTGCT TCCAGAAAAC
 1898 1908 1918 1928 1938 1948 1958
 CCCAGCATCC TTCTGCAAG AGGAGCTTTC TGGAGAGGAG GATGCTGCC TGAGTCACCC ATGAAGACAG
 1968 1978 1988 1998 2008 2018 2028
 GACAGTCTT CAGCCTGAG CTGAGACTGC GGGATGCTC TCGGCTCTG TGCAGGAGG AGGTGGCAGC
 2038 2048 2058 2068 2078 2088 2098
 CCTGTAGGGA AGGAGTCTT TCAAGTTAGC TCAGGAGGCT TGGAAAGCAT CACCTCAGGC CACTGTGCTC
 2108 2118 2128 2138 2148 2158 2168
 ACCCCGATTT AAGCTCTTT TCTCCCAAT GGGATATAA GACCTGTCC TTCTATCAC AAAAGGAGAT
 2178 2188 2198 2208 2218
 TGTGAGCAG AGGAGCAATTA ATAATATG CCAAGTATT AAAAGAGCCG AATTC

Figure
 58. cont

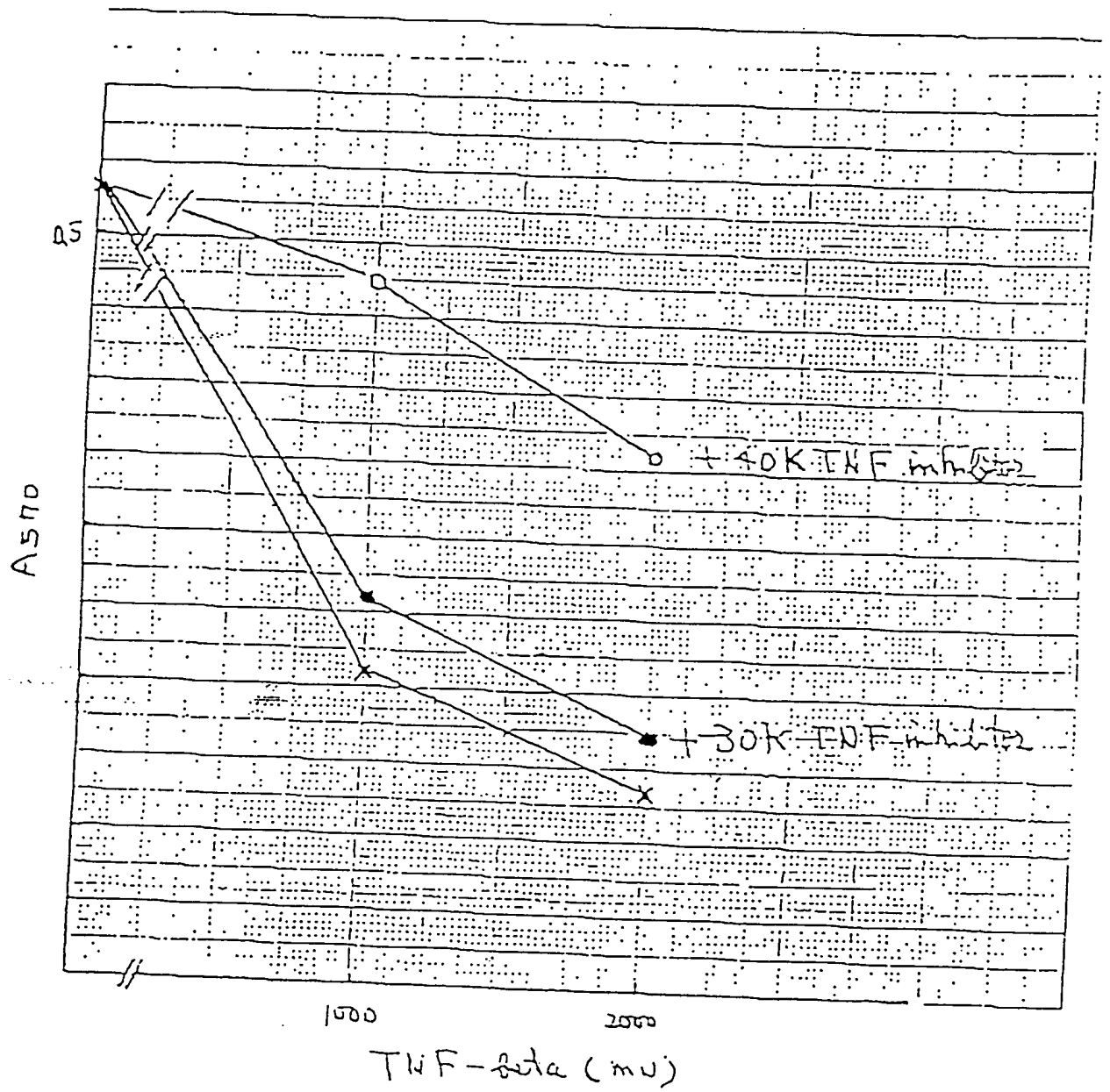


Figure 59

Figure 60

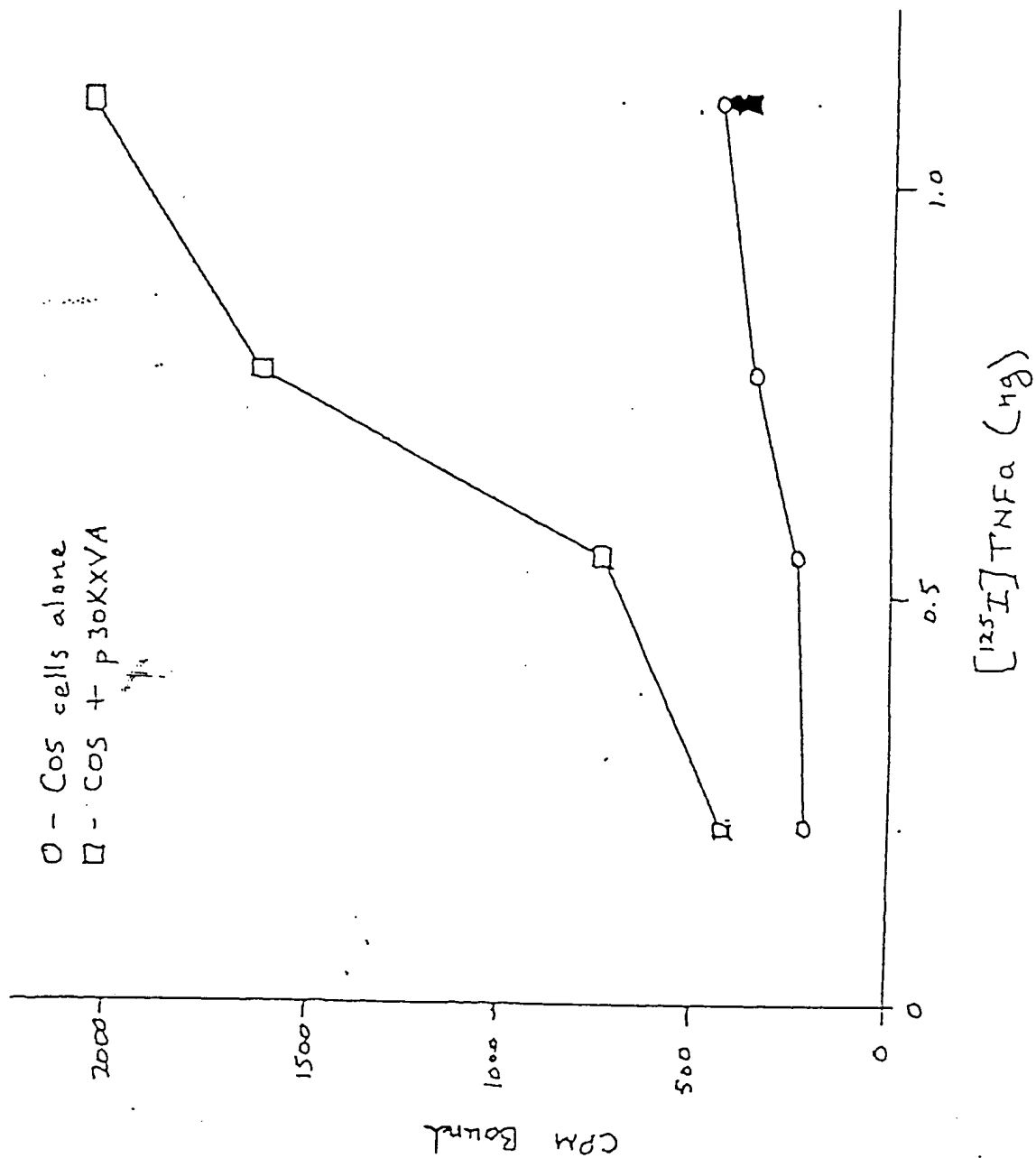
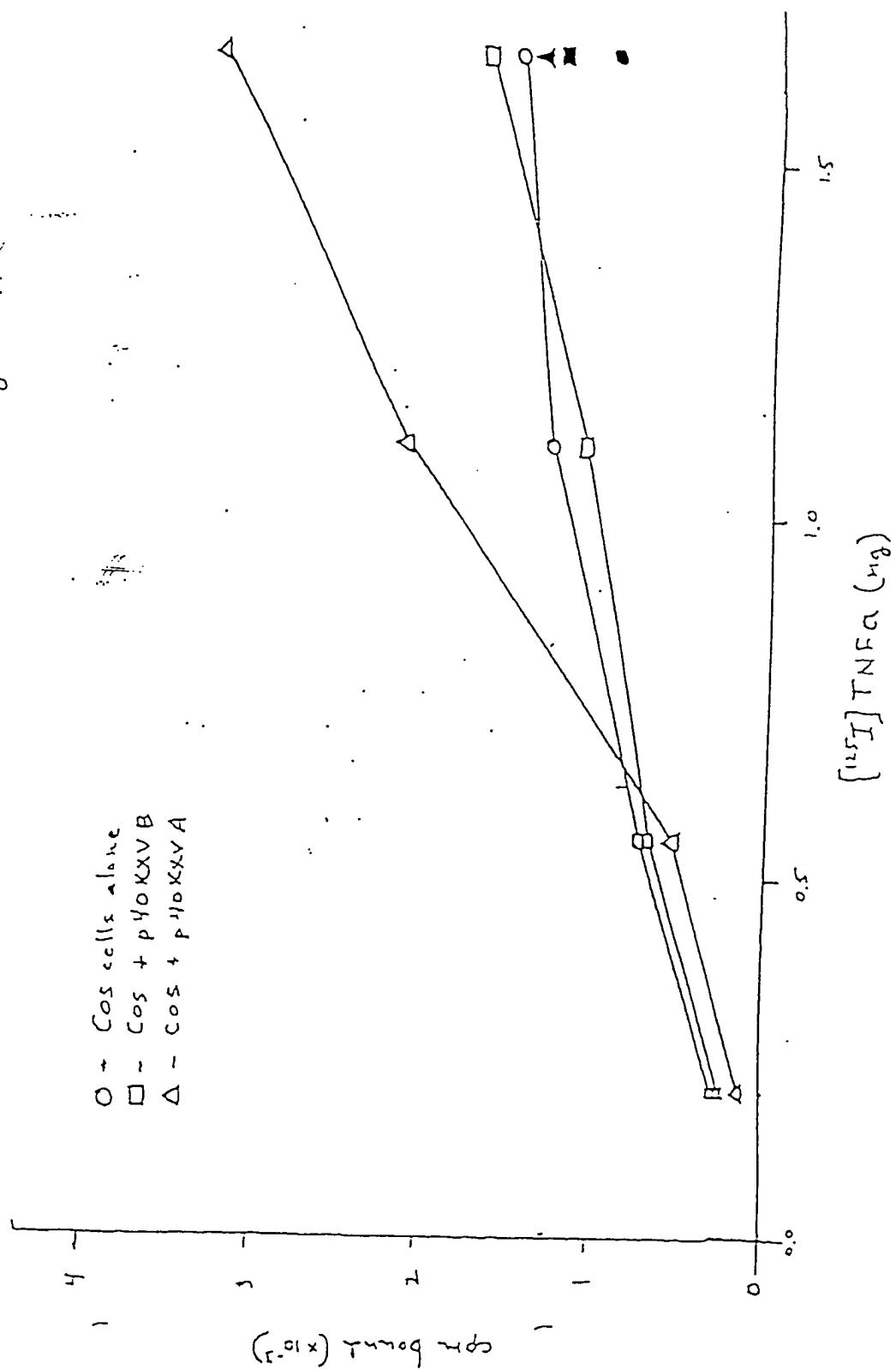


Figure 6A



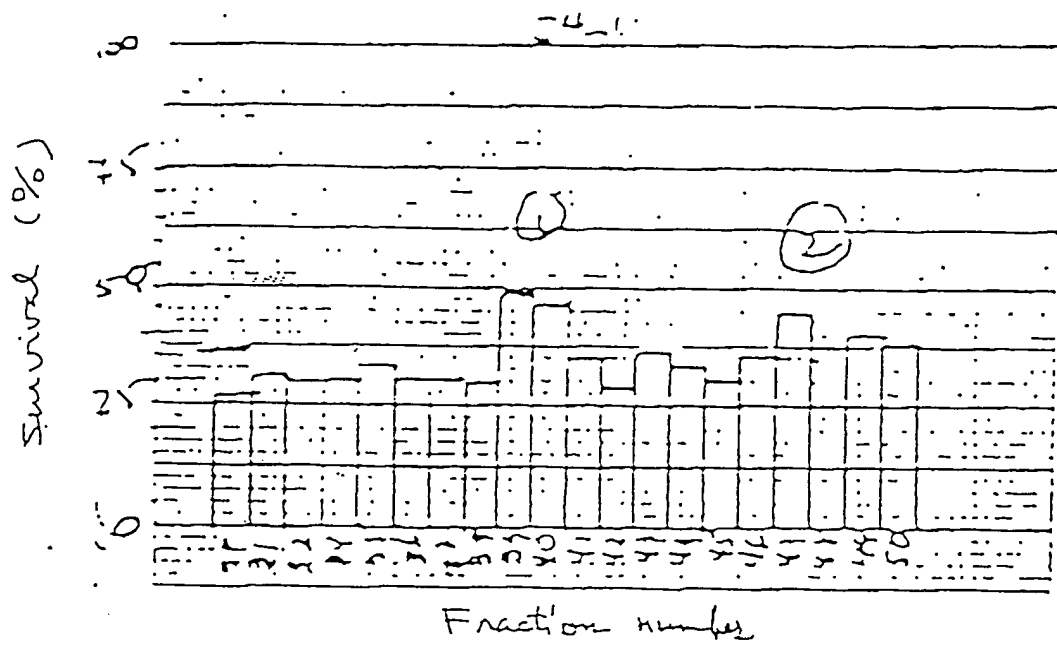


FIG 62

FIG 63

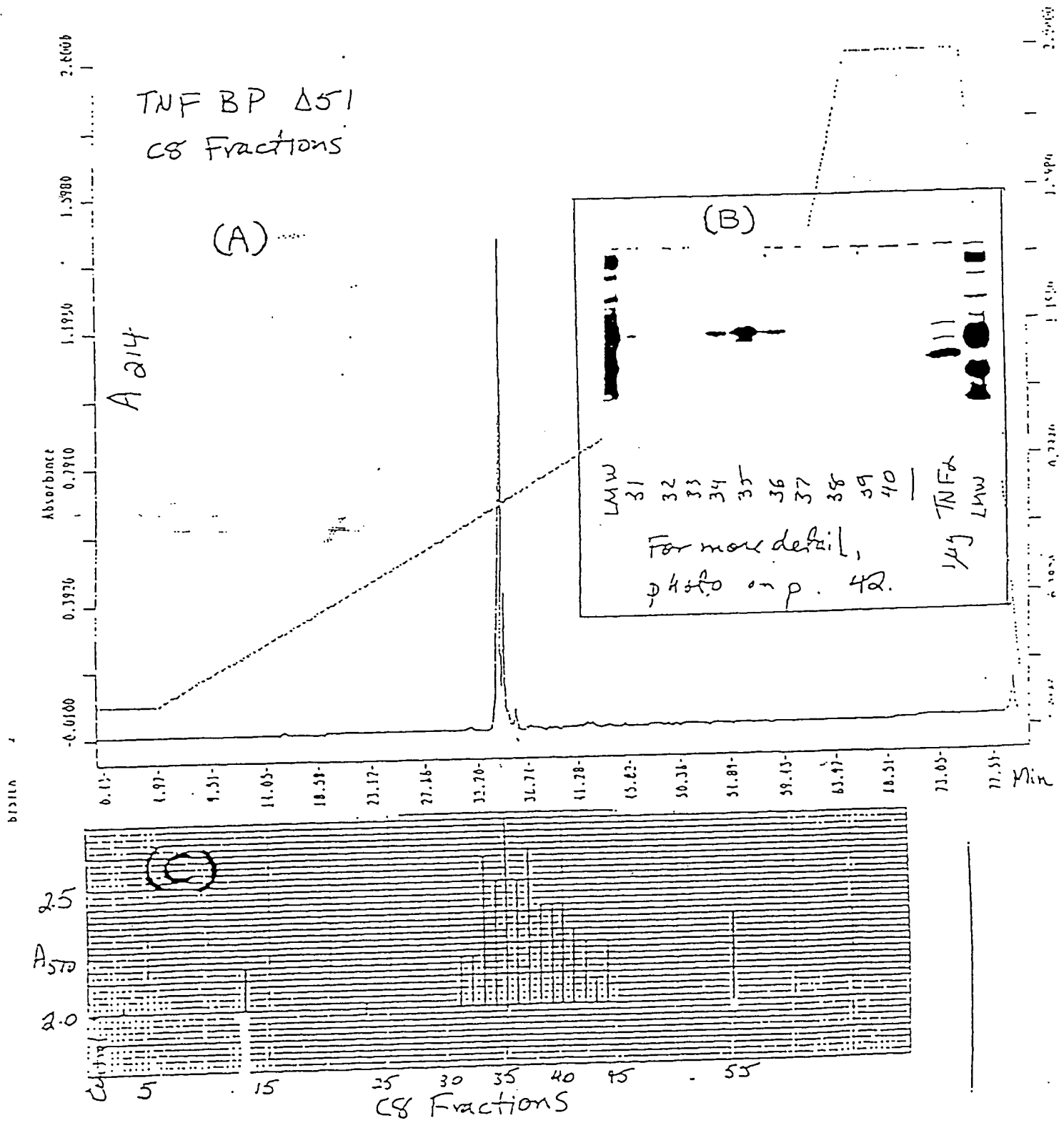


FIG. 64

